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The epidemiology and management of clusters of invasive meningococcal disease in England, 2010–15

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ABSTRACT

Background Guidance for public health management of invasive meningococcal disease (IMD) in in England recommends the use of antibiotic chemoprophylaxis and vaccination. We summarized clinical and epidemiological data collected during routine management of IMD clusters in England.

Methods Data on epidemiology and operational decisions for public health management were reviewed for clusters between April 2010 and December 2015.

Results Clusters were generally 2–3 cases (53/58; 91%) within a single age band <18-years. Nurseries (n = 20, 34%), households/social networks (n = 14, 24%) and schools (n = 10, 17%) were the commonest settings. Chemoprophylaxis alone was used in 36 (58%) clusters, including most serogroup B clusters (31/41; 76%). Chemoprophylaxis and vaccination was used in a further 20 (32%) clusters. Vaccine was delivered promptly (<7 days). Four clusters had cases with onset post-chemoprophylaxis; no clusters recorded cases with onset post-vaccination. No pattern was observed between interventions and setting/population at risk, and interventions were consistent with national guidance. Challenges to management included logistical issues related to intervention delivery.

Conclusions Public health management of IMD clusters presents challenges in decision-making and implementation of interventions. Nonetheless, few cases were observed following intervention. Responses were consistent with national guidance. A systematic data collection tool should be developed to support future evaluation.

Introduction

Invasive meningococcal disease (IMD), caused by infection with *Neisseria meningitidis*, commonly presents as meningitis, septicaemia and other localized invasive presentations.[1] The combination of a high case fatality rate (9% for Europe in 2014)[2] and considerable risk of long-term sequelae[1] generate substantial public concern for just a single case, requiring focused public health management and risk communication. Microbiological characterization into serogroups is based on identified capsular groups (which A, B, C, W, X and Y are

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the most common) with further differentiation by molecular sequence typing.[3]

Following introduction of the meningococcal C (MenC) conjugate vaccine into the UK routine immunization programme for children in November 1999, confirmed cases of IMD caused by serogroup C meningococcus fell dramatically; both directly, by over 90% in immunized age groups, and indirectly, by two-thirds in other age groups due to reduced carriage and exposure.[4] The impact of the introduction of the MenC vaccine in England has also been a reduction in overall IMD incidence with rates remaining relatively stable since (~1 per 100 000 persons), and the greatest burden of disease amongst those aged <1 year and 1–4 years.[5] However, over time, the UK has observed a shift in dominance to serogroup B and the emergence of serogroup W,[5] leading to the replacement of MenC vaccines in the routine infant schedule with a serogroup B vaccine (MenB), and the introduction of a vaccine covering serogroups A, C, W and Y (MenACWY) as an adolescent dose in 2014.[6]

For most, carriage of *N. meningitidis* in the nasopharynx is an asymptomatic event that leads to a systemic protective antibody response,[7] with prevalence peaking in young adults.[8] Transmission is via respiratory aerosol or droplets, and requires substantial contact with a carrier.[9] Consequently, settings where such contact levels occur—living in a 'closed' or 'semi-closed' community (e.g. residential halls or military barracks)—are recognized risk factors for IMD.[10] Transmission from an asymptomatic carrier within the household setting is the most likely route of acquisition for cases of IMD,[11,12] although almost all (>95%) cases in in England and Wales have no recognized transmission links.[13] Household contacts are at highest risk of during the first 7 days after onset of illness in the index case[13] with a low risk for contacts outside of the household.[14,15]

Chemoprophylaxis of household contacts with antibiotics remains the single most effective control measure, through the eradication of the organism from established carriers and from those who may have newly acquired an invasive strain but have yet to progress to infection.[9,16] In the UK, vaccines are available as potential additional interventions for close contacts of IMD cases to reduce the long-term risk of disease.[9] This includes the use of the MenC and MenACWY vaccines and, more recently, the MenB vaccine.[17] However, there remains a need for a stronger evidence-base for the effectiveness of these interventions.[9,16,17]

As part of the routine public health response to IMD clusters, Public Health England (PHE) collects and records clinical and epidemiological details of IMD cases, the population at risk and vaccine uptake. However, data collection is not standardized or mandated. Through a review of information collected for the investigation of IMD clusters in England, we describe the epidemiology and management of clusters in England over a 5-year period and provide insights into the challenges associated with effective management.

Methods

Data collection

Since April 2010, data on IMD cases and clusters in England has been captured on an electronic case and incident management system (HPZone). Data was extracted from HPZone for all clusters of IMD entered between 1 April 2010 and 21 December 2015. Data was collected on the epidemiology of the cluster (number of cases according to diagnostic confidence, age and onset date of cases, meningococcal serogroup, setting and population at risk) and public health management (use of vaccination, including vaccine used and delivery; use of chemoprophylaxis, including antibiotics used and delivery; number eligible and number receiving vaccination and/or chemoprophylaxis; details of decision-making for use of vaccination/chemoprophylaxis) (Supplementary Table S1). Information on the management of clusters was derived from 18 separate data fields.

Case and cluster definitions

Possible case

A clinical diagnosis of meningitis, septicaemia or other invasive disease where the lead public health practitioner, in consultation with a clinician and/or microbiologist, considered that diagnoses other than meningococcal disease were at least as likely.

Probable case

A clinical diagnosis of meningitis, septicaemia or other invasive disease where the lead public health practitioner, in consultation with the physician and microbiologist, considered that meningococcal infection was the most likely diagnosis.

Confirmed case

A clinical diagnosis of meningitis, septicaemia or other invasive disease and at least one of: *N. meningitidis* isolated from a normally-sterile site, Gram-negative diplococci present in a normally-sterile site, meningococcal DNA detected in a normally-sterile site or meningococcal antigen detected in blood, cerebrospinal fluid or urine.

Closed or semi-closed community clusters

Two or more confirmed or probable cases who attended the same educational setting (preschool group, school, college, university) or lived in the same residential setting (household, military barracks, asylum centre, care home) or in other similarly defined social groups that were diagnosed within a 4-week period and were considered at the time of public health action to be caused or likely to be caused by the same meningococcal serogroup.

Wider community clusters

Age-specific attack-rate for a vaccine-preventable meningococcal serogroup within a defined geographical boundary over a 3-month period identified as higher than expected by the managing team and consistent with recommendations in national guidance.[9]

Results

Descriptive epidemiology

There were 94 clusters of IMD recorded between 1 April 2010 and 31 December 2015, two of which extended into 2016. Sixty-two (66%) required public health management and were used as the denominator for the description of public health management. Of these clusters, four were latterly excluded due to either a lack of microbiological evidence to support linkage or discarding of a case that no longer met one of the IMD definitions. Of the 32 clusters that did not require public health management, 23 were not considered for intervention due to information obtained after reporting that meant they no longer met the cluster definition, three were single cases and six were duplicate entries. A total of 58 clusters were included in the descriptive epidemiological analysis (Table 1) (Supplementary Figure).

Table 1 Clusters of invasive meningococcal disease by year, age group of cases, contextual setting and serogroup

Characteristic	*Clusters by year*						*Total*
	2010[a]	*2011*	*2012*	*2013*	*2014*	*2015*	
All clusters	9	11	13	10	6	9	58
Age group							
<1 year only	0	1	0	1	0	0	2
1–4 years only	4	3	5	1	1	2	16
5–9 years only	0	1	1	1	0	1	4
10–17 years only	0	2	1	0	0	0	3
0–18 years only	3	1	5	3	1	2	15
≥18 years only	0	2	1	1	3	3	10
All ages	2	1	0	3	1	1	8
Contextual setting							
Nursery	4	4	6	3	1	2	20
Household/social network	2	1	3	3	3[b]	2	14
School	1	3	3	1	0	2	10
College/university	0	2	0	0	1[b]	3	6
Community	1	1	0	1	1	0	4
Other[c]	1	0	0	1	0	0	2
Care home	0	0	0	1	1	0	2
Hospital	0	0	1	0	0	0	1
Serogroup							
B	6	11	11	6	2	4	40
C	0	0	0	0	2	2	4
W	0	0	1	2	1	1	5
Y	2	0	0	0	0	1	3
Untyped	1	0	1	2	1	1	6

[a]Data from 1 April 2010.

[b]One cluster involving two settings.

[c]Visitor attraction (2010) and caravan site (2013).

There was an average of 10 (range 6–13) IMD clusters recorded per year between 2011 and 2015 (Table 1). The number of reported clusters mirrored the seasonal distribution of IMD cases (Spearman's rank correlation coefficient, $r_s = 0.615$, $P = 0.001$) with some geographical variation (Fig. 1). Clusters comprised a total of 148 cases, of which 79% ($n = 117$) were laboratory-confirmed. The majority of clusters consisted of two ($n = 39$, 67%) or three ($n = 14$, 24%) cases; four clusters consisted of four cases and one cluster of 12 cases.

Forty clusters (69%) consisted only of cases aged <18 years; 64% (16/25) were restricted to cases aged 1–4 years (Table 1). A further 10 clusters consisted only of those aged ≥18 years and another eight clusters considered of cases aged both <18 and ≥18 years. Nurseries ($n = 20$, 34%), households or social networks ($n = 14$, 24%) and schools ($n = 10$, 17%) were the most common settings (Table 1). There were no clusters identified within the childminder setting.

Serogroup B accounted for 69% (40/58) of clusters, with the highest numbers of clusters reported in 2011–12 (11 each year) and then falling to an average of four clusters per year for 2013–15. Typing information was not available for six clusters. Of the confirmed cases which were part of a cluster, 77% (90/117) were serogroup B (Table 2). The percentage of laboratory-confirmed cases nationally that were within clusters (all serotypes: 117/4723, 2.5%) was similar for serogroup B (90/3450, 2.6%) and for all other serogroups combined (27/1273, 2.1%) ($\chi^2 = 0.69$, $P = 0.407$). There was no evidence of a statistically significant trend in the proportion of quarterly laboratory-confirmed cases that were part of clusters (Poisson regression; all serogroups, serogroup B, all other serogroups: each $P > 0.05$). Fifty percent (45/90) of cases within clusters of serogroup B were aged 1–4 years (Table 2). The vast majority of clusters of serogroup B (88%, 35/40) involved cases aged <18 years and 60% (24/40) were either in nurseries ($n = 17$) or schools ($n = 7$) (Table 2).

The majority of clusters (57%; 33/58) had a duration (interval in days between onset of the first and last case) of ≤7 days (median = 7, range 0–151). Eight clusters extended over 30 days and included ≥3 cases; the setting for these clusters were nurseries (three clusters), colleges/universities (two clusters), community increases (two clusters) and a household/social network (one cluster). Only four clusters included cases with onset dates reported after the date of implementation of chemoprophylaxis; no situations recorded cases with onset after vaccination.

Management of clusters

Use of interventions

Antibiotic chemoprophylaxis only was used as an intervention for 36/62 (58%) clusters (an additional three clusters were managed with chemoprophylaxis but information on use of vaccines was not available) and a further 20 (32%)

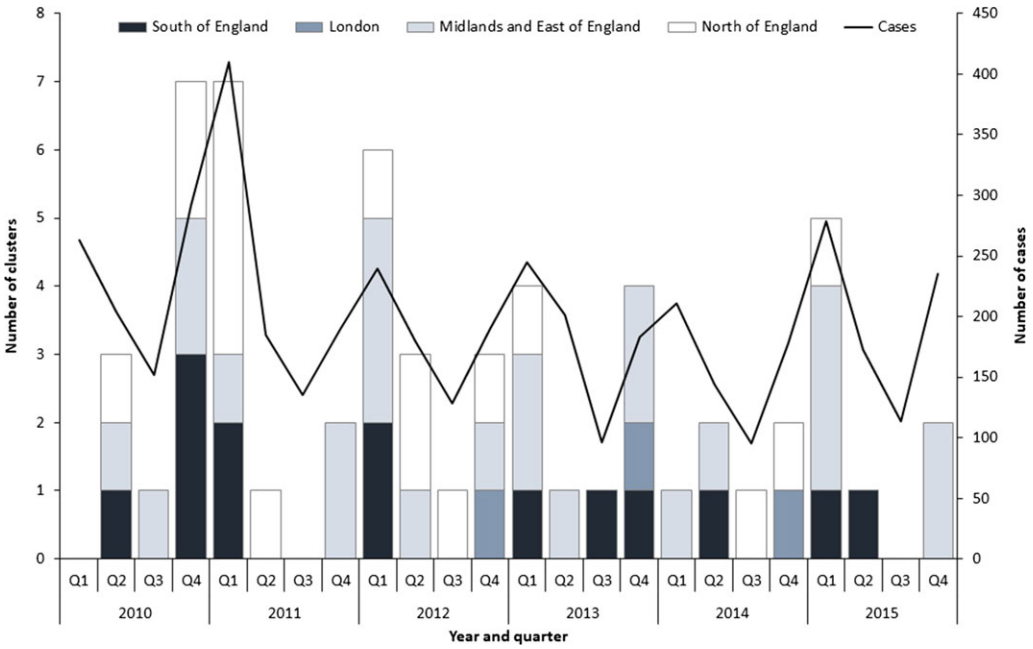

Fig. 1 Laboratory-confirmed cases and clusters of invasive meningococcal disease in England. Cases are those confirmed at the Public Health England Meningococcal Reference Laboratory. Q1 = January–March; Q2 = April–June; Q3 = July–September; Q4 = October–December.

Table 2 Clusters of invasive meningococcal disease by serogroup and contextual setting and age group of cases

Characteristic	*Serogroup*				
	B	*C*	*W*	*Y*	*Not typed*
Number of clusters					
Contextual setting					
Nursery	17	0	1	0	2
Household/social network	9	1[a]	1	0	3
School	7	2	0	0	1
College/university	4	1[a]	0	1	0
Community	2	1	0	1	0
Other[b]	1	0	0	1	0
Care home	0	0	2	0	0
Hospital	0	0	1	0	0
All settings	***40***	***4***	***5***	***3***	***6***
Number of cases					
Age group					
<1 year	5	0	1	1	1
1–4 years	45	2	2	1	13
5–9 years	14	3	0	0	8
10–17 years	9	1	0	1	3
≥18 years	17	2	7	3	5
All ages	***90***	***8***	***10***	***6***	***34***

[a]One cluster involving two settings.

[b]Visitor attraction (serogroup Y) and caravan site (serogroup B).

Table 3 Management of invasive meningococcal disease clusters by serogroup, context and age group of population at risk

Characteristic	*Interventions*			*Total*
	Chemoprophylaxis and vaccination	*Chemoprophylaxis only*	*None*	
All situations	20	39[a]	3	62
Serogroup				
B	6[b]	32[c]	3	41
C	6	0	0	6
W	5	0	0	5
Y	3	0	0	3
Not typed	0	6[c]	0	6
N/A	0	1	0	1
Context[d]				
Nursery	3	15	2	20
Household/ social network	6	9[e]	1	16
School	3	8	0	11
College/ University	2	4	0	6
Community	2	2	0	4
Other	1	1	0	2
Care Home	2	0	0	2
Hospital	1	0	0	1
Workplace	1	0	0	1
Age group				
<1 year only	0	2	0	2
1–4 years only	3	12	1	16
5–9 years only	1	3	0	4
10–17 years only	0	3	0	3
<18 years only	6	4	0	10
≥18 years only	3	10[c]	2	15
All ages	7	5[c]	0	12

[a]Information on use of vaccination missing for three clusters.

[b]One cluster managed with MenACWY vaccine.

[c]Information on use of vaccination missing for one cluster.

[d]One situation included two settings.

[e]Information on use of vaccination missing for two clusters.

clusters were managed with a combination of chemoprophylaxis and vaccination (Table 3). Three clusters were not managed with either chemoprophylaxis or vaccination (Table 3). There was no clear pattern to the choice of intervention by context or the age group of the population at risk (Table 3).

Chemoprophylaxis only was used where: typing information was not available (four clusters), for a cluster latterly determined not to be a true cluster, and for the majority of serogroup B clusters (31/41, 76%). There were three serogroup B clusters (two in a nursery and one in a household/social setting) where only immediate contacts of individual cases were managed with chemoprophylaxis.

All clusters of meningococcus serogroup C, W and Y were managed with a combination of chemoprophylaxis and vaccination (Table 3). Only 15% (6/41) of the serogroup B clusters were managed with vaccination and chemoprophylaxis; representing five of the six clusters that occurred during 2014–15 (i.e. after the introduction of the MenB vaccine) and one cluster managed in 2010 (a family with underlying immunological disease where the MenACWY conjugate vaccine was offered to protect against other serogroups). The two serogroup B clusters that occurred after 2014 and where vaccination was not offered both occurred in a college/university setting. The rationale for not offering vaccination was available for one of these clusters and was based on strain characterization of isolates from two cases that indicated a lack of genetic relatedness.

Other interventions were employed for 14 (23%) clusters; including information and awareness-raising to the population

at risk, healthcare professionals and the wider community. One cluster at a university involved working with the local healthcare community to deliver vaccination clinics for eligible staff and students to improve uptake amongst the wider population considered to be at risk.

The total number of contacts eligible for chemoprophylaxis was available for 80% (47/59) of clusters managed with chemoprophylaxis. In two additional clusters only household members were offered chemoprophylaxis but the household size was not recorded. The size of the population at risk ranged from 0 to 5 300 (median = 46, interquartile range [IQR] = 13–126). The situation with 5 300 persons at risk involved a holiday park and included not just close contacts of cases but all staff and visitors on site at the same time as the cases. For the majority of clusters where data was available, all eligible contacts received chemoprophylaxis (70%, 29/42). Reasons for failure to treat all eligible contacts included absence from school, failure to attend intervention events and refusal/lack of consent.

Delivery of interventions

Chemoprophylaxis and vaccination were delivered in a range of settings. For chemoprophylaxis, this included the implicated institution (20 clusters), the General Practice (five clusters), the hospital (four clusters) and a combination of hospital and General Practice (five clusters). Management of two clusters involved bespoke clinics set-up to offer chemoprophylaxis to nurseries. Delivery of chemoprophylaxis in the community was completed by a combination of staff from multiple organizations, including staff from the National Health Service, PHE and other local health organizations. Of the clusters where vaccine was used and data was available, vaccine was delivered within primary care (57%; 7/13) or the implicated setting (43%; 6/13).

Chemoprophylaxis was implemented within 48 h (range 0–66 days) of the decision to intervene for 80% of clusters (33/38 with available data). Two clusters reported a delay of over 30 days: one of these involved four cases within a household setting over a 2 month period where a diagnosis of underlying immunological disease informed additional control measures. The second cluster involved two probable cases 14 days apart within a household setting where the population at risk spanned five households.

For those clusters where data was available (11/20), the number of contacts eligible for vaccination ranged from 0 to 188 (median = 24; IQR 10–91). Vaccine was provided within 7 days of the decision to vaccinate for nine of the 10 situations where data were available; for four situations vaccination occurred within 48 h. For eight of these clusters, the number of contacts eligible for vaccination was the same as those eligible for chemoprophylaxis. Eligible contacts received vaccination for seven of the nine (78%) clusters where the number of contacts vaccinated was recorded.

Challenges to management

Both decision-making and operational challenges during management of clusters were documented for 12 IMD clusters. The major challenge was the inability to clearly define the population at risk (for example, two cases in a school but not in the same year group or social network). Other documented challenges included a lack of clear eligibility for vaccination following new guidance for meningococcal B clusters, difficulty in tracing all contacts and atypical microbiological findings (each reported for one cluster).

Operational challenges to the delivery of interventions (22 clusters) included resource constraints (difficulty sourcing vaccine or antibiotics, particularly syrup preparations; limited nursing staff available to deliver intervention; uncertainty about funding the intervention, specifically in one instance where students were asked to pay for the prescription), logistics (organizing a large-scale intervention within a very short time frame), communication (rapidly and effectively contacting families and obtaining consent), and having legal frameworks in place to allow supply of medicines (Patient Group Directions; PGD). Two of the five serogroup B clusters managed with vaccination reported issues of sourcing and cost of the vaccine as a challenge to delivery. Both clusters were from 2014, and noted particular uncertainty at that time given the new recommendations for use of the MenB vaccine.

Where challenges to the overall management of the cluster were documented (16 clusters), parental and public anxiety and issues of effective communication were most commonly reported (eight clusters). Other challenges included a lack of clarity on roles and responsibilities of key stakeholders and where complex epidemiology of the cluster made decisions about the need to extend management of the cluster difficult. Actions taken included developing a suite of communications material for parents, public and health professionals, including signposting and use of material produced by meningitis charities. Full and frank debriefs were also noted to be important to clarify roles and responsibilities and to work through logistics for similar situations that may occur in the future (this included developing PGD, identifying stocks of chemoprophylaxis, and mechanisms for obtaining large volumes of vaccine). Solutions adopted to ensure effective delivery of interventions included the use of smart technology (text messages to contact parents) to support rapid communication and to improve pre-completion of consent, often supplemented by active follow-up.

Discussion

Main findings of this study

This study describes the epidemiology and effective management of IMD clusters in England and provides insights into the challenges encountered during management. Clusters of IMD most commonly occurred in closed settings such as nurseries, schools and households, with the majority involving ≤3 cases. No clusters were reported in a childminder setting and community-wide increases were very uncommon. All but three clusters involved the provision of antibiotic chemoprophylaxis, with or without vaccination, to the wider population at risk, delivered within 48 h for 80% of managed clusters. Where vaccine was used, implementation occurred within seven days for all but one cluster. Control measures appeared effective in limiting spread: only four clusters included cases with onset dates reported after the date of implementation of chemoprophylaxis; no situations recorded cases with onset after vaccination. The main documented challenges were logistical, related to the delivery of antibiotics and vaccine.

What is already known on this topic

Clusters of IMD require timely public health action to prevent further transmission, particularly the prompt vaccination of contacts. Effective public health action is primarily through chemoprophylaxis of close contacts with antibiotics. Vaccination is considered where typing indicates risk from a vaccine-preventable strain, although use of vaccine is known to have considerable resource implications.

What this study adds

Clusters of IMD were generally small (≤3 cases) affecting children and young adults, with children aged 1–4 years being the most affected age group. As is expected given this age group, clusters most commonly occurred in nurseries, schools and households. Given predominance in this age group and within closed settings, and the known risk factors for person-to-person transmission of *N. meningitidis*, it is not unexpected that community wide increases were very uncommon. Although serogroup B was isolated in over two-thirds of reported clusters, the number of serogroup B clusters decreased after 2013, with a concomitant increase in the number of clusters due to serogroups Y, W and C.

All but three clusters involved the provision of antibiotic chemoprophylaxis, with or without vaccination, to the wider population at risk. A lack of systematic data collection limits the use of current data for the evaluation of the impact of public health interventions for IMD clusters. Challenges to management were largely logistical, related to local responsibilities and complexities of sourcing antibiotics, vaccines and staff to deliver the intervention to a very short timescale. It is nonetheless encouraging that interventions intended to reduce the risk of serious infection and to interrupt transmission were promptly delivered.

Communication and justification of key decisions to the population at risk, wider members of the public and healthcare professionals, was another challenge. Refusal or failure to accept interventions were reported as primary reasons for sub-optimal uptake in two-thirds of clusters where data was available. A qualitative evaluation of acceptability, knowledge and attitudes (of both the population at risk and healthcare professionals) may inform how information can be best communicated and interventions delivered to maximize uptake.

Limitations of this study

This study utilized data recorded routinely for public health management. As such, data fields did not match the exact requirements of their secondary use in this study. Despite good overall completion, information was inconsistently presented or stated as not available or not clear for a number of data fields, including the population at risk. The description and number of contacts within each population at risk group was only provided in full for 27 clusters. Information on the management of clusters was derived from 18 data fields, with only six of these fields completed for all situations: fields that were least well completed were date of implementation (88%), how chemoprophylaxis was delivered (88%) and other interventions (92%). Information on how vaccine or chemoprophylaxis was sourced and administered was also poorly recorded. Not all household clusters of IMD are entered onto the system, meaning that there may be an under-representation of clusters.

Although the use of routine cluster management data provides invaluable insight into the epidemiology of clusters of IMD, data quality limits its use in formal evaluation of the effectiveness of vaccines in cluster management. Further work is required to robustly evaluate the use of vaccines (particularly, the 4CMenB [Bexsero®] vaccine), for management of IMD clusters and to address gaps in the evidence base. Where typing results were not available, it is possible that clustered cases were not epidemiologically linked.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online.

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